REMARKS

The claims which are before the examiner are now 1-26. Claims 1-3 and 14 have been amended. Claims 27, 28 and 30-38 have been canceled with the proviso that applicants reserve the right to file divisional applications with respect to any subject matter withdrawn from consideration under the provisions discussed in *Studiengesellschaft Kohl mbH v. Northern Petrochemical Co.*, 784 F.2d 351, 355,228 USPQ 837, 840(Fed. Cir.) *cert. dismissed* 478 U.S. 1028 (1986).

Preliminarily, the examiner is thanked for his kind suggestions and observations.

The amendments to the specification merely delete translator's notes (i.e. [sic] and/or [lacuna]) and correct syntax errors. No new matter has been added.

It is submitted that applicants have amended the claims to overcome the 35 USC § 112, second paragraph.

The "or's" have been added as kindly suggested by the examiner in his designations, starting at page 6, a)through l), l) through q), and s) through x). In addition, an "or" has been added before the last heterocyclic ring under R^5.

Regarding objection j), it is submitted that the commas added before and after the expression, "independently of one another".

Regarding k), the examiner's suggestion has been adopted.

Regarding r), the phase has been rewritten in order to make it clear that the phenyl carries the substituent(s) $NR^{k1}R^{k2}$.

Regarding y), the examiner's suggestion has been adopted.

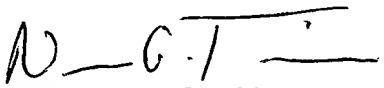
Applicants would also like thank the examiner for his recognition that the claims are drawn on allowable subject matter. Should the examiner have any other problems or suggestions, she is welcome to contact the undersigned in order to expedite the prosecution of this application.

Accordingly, allowance is respectfully solicited.

Please charge any shortage in fees due in connection with the filing of this paper, including Extension of Time fees to Deposit Account No. 11-0345. Please credit any excess fees to such deposit account.

Respectfully submitted,

KEIL & WEINKAUF



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VERSION WITH MARKINGS TO SHOW CHANGES MADE IN THE SPECIFICATION

Page 1, lines 24-38, should read as follows:

It is known that free radicals such as superoxided anion, NO and hydrogen peroxide may lead to DNA damage in cells and thus activate PARP. The formation of large amounts of free radicals in observed in a number of pathophysiological states, and it is assumed that this accumulation of free radicals [[sic]]lead or contribute[[sic]] to the observed cell or organ damage. This includes [of [sic]], for example, ischemic states of organs as in stroke, myocardial infarct (C. Thiemermann et al. , *Proc. Natl. Acad. Sci.* USA 1997, 94, 679-683) or ischemic of the kidneys but also reperfusion damage as occurs, for example, after lysis of myocardial infarct (see above C. Thiemermann et al.). Inhibition of the enzyme PARP might accordingly be a means of art least partly preventing or moderating this damage. PARP inhibitors might thus represent a novel therapeutic principle for treating a number of diseases.

Page 2, lines 8-16 should read as follows:

It has likewise been discovered that PARP is involved in immunological disorders or diseases in which the immune system plays an important part, such as, for example, rheumatoid arthritis and septic shock, and that PARP inhibitors may show a beneficial effect in the course of the disease (H Kröger et al. *Infammation* [[sic]] 1996, 20, 203-215; W. Eherlich et al. *Rheumatol. Int.* 1995, 15, 171-172; C. Szabo et al., *Proc. Natl. Acad. Sci. USA* 1998, 95, 3867-3872; S. Cuzzocrea et al. *Eur. J. Pharmacol.* 1998, 342, 67-76)

Page 2, line 44 - Page 3, line 26 should read as follows:

The synthesis of 2-phenylbenzimidazyl-4-amides [[sic]] has been described in J. Chem. Soc. Perkin Trans 1, 1979, 2303-2307. Analogous compounds which have a substituted alkyl chain on the amide residue and are said to have a cytotoxic effect are mentioned in J. Med. Chem. 1990, 33, 814-819. WO 97/04771 mentions benzimidazole-4-amides [[sic]] which inhibit PARS. In particular, derivatives described therein as active have a phenyl ring in position 2, and the phenyl ring may also be substituted by simple substituents such as nitro, methoxy and CF_3. Although some of these substances show good inhibition of the enzyme PART, the derivatives described therein have the disadvantage that they show little or no solubility in aqueous solutions and thus cannot be administered as aqueous solution.

In a number of therapies, such as stroke, the active substances are administered intravenously as infusion solution. For this purpose it is necessary to have available substances, in this case PARP inhibitors, which have adequate solubility in water at physiological pH values of close pH values(e.g. pH valued of 5-8), so that an infusion solution can be prepared. Many of the PARP inhibitors described, especially the more effected PARP inhibitors, have the disadvantage, however, that they have only low or no solubility in water at these pH values and thus are unsuitable for intravenous administration. Active substances of this type can be administered only with ancillary substances intended to promote solubility in water (cf. WO 97/04771). These ancillary substances, for example polyethylene glycol and dimethyl [[sic]] sulfoxide, frequently

cause side effects or are not tolerated. Very effective PARP inhibitors with adequate solubility in water have not previously been described.

Page 7, line 42- page 8, line 4 should read as follows:

R^9 is hydrogen, $COCH_3$, $CO\text{-}O\text{-}C_1\text{-}C_4$-alkyl, $COCF_3$, branched and unbranched, $C_1\text{-}C_6$-alkyl, it being possible for one or two hydrogens of the $C_1\text{-}C_6$-alkyl radical to be substituted in each case by one of the following radicals: OH, $O\text{-}C_1\text{-}C_4$-alkyl and phenyl, and for the phenyl ring also to carry one or two of the following radicals: iodine, chlorine, bromine, flourine, branched or unbranched $C_1\text{-}C_6$-alkyl, nitro, amino, $C_1\text{-}C_4$-alkylamino, $C_1\text{-}C_4$-dialkylamino, OH, $O\text{-}C_1\text{-}C_4$-alkyl, CN, CF_3, $SO_2\text{-}C_1\text{-}C_4$-alkyl, and [[sic]]

Page 8, line 25 should read as follows:

R^{23} are [[sic]] hydrogen, $C_1\text{-}C_4$-alkyl or phenyl, and

Page 8, line 31 should read as follows:

m,o is, [[sic]] independently of one another, 0, 1 or 2, and

Page 8, line 42 should read as follows:

R^{43} are [[sic]] $C_1\text{-}C_4$-alkyl or phenyl, and

Page 12, lines 27-35 should read as follows:

For R^3 being

the particularly preferred meaning of R^{31} is[is [sic]] hydrogen or $-(CH_2)_p-R^5$, where

Page 13, lines 8-16 should read as follows:

R^{52} can be [[sic]]hydrogen, branched and unbranched C_1-C_6-alkyl, where one hydrogen of the C_1-C_6-alkyl radical may be substituted by one of the following radicals: OH, O-C_1-C_4-alkyl and phenyl, and where the phenyl ring may also carry one or two of the following radicals: chlorine, bromine, fluorine, branched and unbranched C_1-C_4-alkyl, nitro, amino, C_1-C_4-alkylamino, C_1-C_4-dialkylamino, OH, O-C_1-C_4-alkyl, CN, SO_2-C_1-C_4-alkyl.

Page 15, lines 36-41 should read as follows:

Introduction of the R1 [[sic]] radical on the benzimidazole residue in I (R_1 =H) takes place under customary alkylation conditions as it[[sic]] for example in J.Het.Chem. 1995, 32, 707f and in Tetrahedron 1994, 50, 5535), although it is necessary to employ the reactant R_1-L (L=leaving group Cl, Br and I).

Page 16, lines 23-47 should read as follows:

As an alternative to the benzaldehydes V shown in scheme 1, it is also possible to employ benzoic acids such as XI (see scheme 2) or benzonitriles such as XIII (see scheme 3) in place of the benzaldehyde. The preparation of these derivatives is analogous to the preparation of the substituted benzaldehydes V. Starting from XI, the condensation to VII takes place in two stages. Firstly, the benzoic acid XI is reacted with the aniline VI in a peptide-like coupling to give the amide XII. Conventional

Houben-Weyl, Methoden der Ogranischen Chemie, 4th Ed. E5, chapter V, or C.R. [[sic]] Larock, Comprehensive Organic Transformations, VCH Publisher, 1989, page 972 et seq. The ring closure takes place [[sic]] to the benzimidazole then takes place at elevated temperature, for example 60 to 180°C, with or without solvent such as dimethylformamide, with the addition of acids such as acetic acid, or directly in acetic acid itself.

Reaction of the phenylenediamine VI with ah benzonitrile XIII likewise takes place under conventional conditions. This can be carried out in solvents such as dimethylformamide with the addition of acids at elevated temperatures such as 60 to 200°C. However, it is also possible to use the conventional methods for preparing amidines from benzonitriles, as described in [in[sic]] Houben-Weyl, Methoden der Ogranischen Chemie, E5, p. 1304 f., J. Amer. Chem Soc. 1957, 427 and J. Org. Chem. 1987, 1017.

Page 21, lines 10-35 should read as follows:

The polyADP-ribosylatable table preferably used in the detection method is a histone protein in its native form or a polyADP-ribosylatable equivalent derived therefrom.. A histone preparation supplied by Sigma (SIGMA catalog No. H-7755; histone type II as [[sic]] from calf thymus, Luck JM et al., J. Biol Chem., 235, 2801 (1960)) was used by way of example. It is possible in principle to use all types of proteins or parts thereof amenable to polyADP-ribosylation of PARP. These are preferably nuclear proteins, e.g. histone, DNA-polymerase, telomerase or PARP itself.

Synthetic peptides derived from the corresponding proteins can also act as target.

In the ELISA assay [[sic]] it is possible to use amounts of histones in the range from 0.1 µm/well to 100 µm/well, preferably 1µm/well to 10 µm/well. The amounts of the PARP enzyme are in the range from 0.2 pmol/well to 2 nmol/well, preferably from 2 pmol/well to 200 pmol/well; the reaction mixture in each comprising 100 µl/well. Reductions to smaller wells and correspondingly smaller reaction volumes are possible. In the HTRF assay, identical amounts of PART are employed, and the amount of histone or modified histones is in the range from 2 ng/well to 25 µg/well, preferably 25 ng/well to 2.5 µg/well, the reaction mixture in each case comprising 50 µl/well. Reduction to smaller wells and correspondingly smaller reaction volumes are possible.

Page 21, line 40 - page 22, line 6 should read as follows:

Various types of damaged DNA can function as activators. DNA damage can be produced by digestion with DNAases [[sic]] or other DNA-modifying enzymes (e.g. restriction endocucleases), by irradiation or other physical method or chemical treatment of the DNA. It is further possible to simulate the DNA damage situation in a targeted manner by using synthetic oligonucleotides. In the assays indicated by way of example, activated DNA from calf thymus was employed (SIGMA, Product No. D4522, CAS: 91080-16-9, prepared by the method of Aposhian and Kornberg using calf thymus DNA (SIGMA D-1501) and deoxyribonuclease type I (D-4263). Aposhian HV and Kornberg A., J. Biol. Chem., 237, 519 (1962)). The activated DAN was used in a concentration range of 0.1 -1000 µg/ml, preferably from 1 to 100 µg/ml, in the reaction

step.

Page 23, line 45 to page 24, line 12 should read as follows:

In a homogenous assay, all the components are also resent during the measurement. Whereas this has advantages for carrying out the assay (rapidity, complexity), it is necessary to preclude interference by assay components (inherent fluorescence, quenching by dyes etc.). HTRF precludes such interference by time-delayed measurement at two wavelengths (665nm, 620 nm). The HTRF fluorescence [[sic]] has a very long decay time and time-delayed measurement is therefore possible. There is no longer any interference from short-lived background fluorescence (e.g. from assay components or inhibitors of the substance bank). In addition, measurement is always carried out, at two wavelengths in order to compensated for quench effects of colored substances. HTRF assays can be carried out, for example, in 96- or 384-well microtiter plate format and are evaluated using a Discovery HTRF Microplate Analyzer (Packard Instruments).

Page 24, lines 21-22 should read as follows:

b1) contacting the immobilized PARP homolog [[sic]] with an analyze in which at least one binding partner is suspected; and

Page 25, lines 1-4 should read as follows:

The following were used, inter alia, anti-poly(ADF-ribose) antibodies (polyclonal antiserum, rabbits), BIOMOL; order No. SA-276. Anti-poly(ADP-ribose) antibodies (monoclonal, mouse; Clone 10H; hybrioma [[sic]] supernatant, affinity-purified).

Page 25, line 10 should read as follows:

b) ELISA assay [[sic]]

Page 26, line 43 - page 27, line 9 should read as follows:

b) [[sic]] HTRF (homogenous time-resolved fluorescence) assay

In the [HTFR [sic]] PARP assay according to the invention, histones, as target proteins for modification by PARP, are labeled indirectly with an XL665 fluorophore. The antibody is directly labeled with a europium cryptate. If the XL665-fluorophore is in the direct vicinity in space, which is ensured by binding to the poly(ADP-ribose) on the histone, then energy transfer is possible. The emission at 665 nm is thus directly proportional to the amount of bound antibody, which is in turn is equivalent to the amount of poly(ADP-ribose). The measured signal thus corresponds to the PARP activity. The materials use are identical to those used in the ELISA assay [[sic]] (see above) unless not expressly indicated.

Page 27, lines 29- 31 should read as follows:

- 10 µl of PARP solution in PARP HTRF reaction buffer (50 mM Tris-HCl pH 8.0, 10 mM MgCl12 [[sic]], 1 mM DTT) with 20 ng of PARP (human or bovine)

Page 28, lines 12-15 should read as follows:

Measurement was then possible after 30 minutes (up to 4 hours). The measurement took place in a "Discovery HTRF Microplate Analyzer" (Packard Instruments). The K_i values were calculated as described fro the ELISA assay [[sic]].

Page 29, lines 1-20 should read as follows:

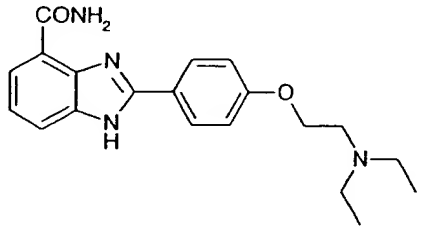
and partial epileptic seizures such as temporal lope [[sic]], and complex partial seizures, and further for the treatment and prophylaxis of damage to the heart after cardiac ischemia and damage to the kidneys after renal ischemia, for example of acute renal insufficiency, of acute kidney failure or of damage occurring during and after a kidney transplant. The compounds of the general formula I can further be used treat acute myocardial infarct and damage occurring during and after medical lysis thereof (for example with TPA, Reteplase, streptokinase or mechanically with a laser or Rotablator) and of microinfarcts during and after heart valve replacement, aneurysm resections and heart transplants. It is likewise possible to use the present 2-phenylbenzimidazoles I for treatment in cases of revascularitzation of critically narrowed coronary arteries, for example in PCTA and bypass operations, and critically narrowed peripheral arteries, for example leg arteries. In addition, the 2-phenylbenzimidazoles I can be beneficial in the chemotherapy of tumors and metastasis thereof and can be used to treat inflammations and rheumatic disorders such as, for example, rheumatoid arthritis.

Page 29, Table 1, column 2, row 2 lines 33-36 should read as follows:

Permanent MCAO ("middle cerebral artherial [[sic]] occlusion")

Page 32, lines 1-12 should read as follows:

2-(4-(2-(N,N-Diethylamino) eth-1-yloxy)phenyl) benzimidazole-4-carboxamide



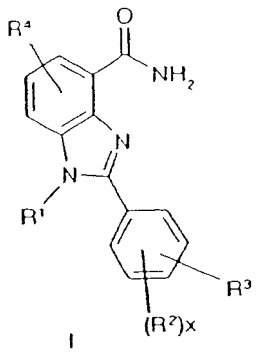
a) 4-(2-(N,N-diethylaminoeth-1-yloxy) benzaldehyde [[sic]]

VERSION WITH MARKINGS TO SHOW CHANGES MADE IN THE CLAIMS

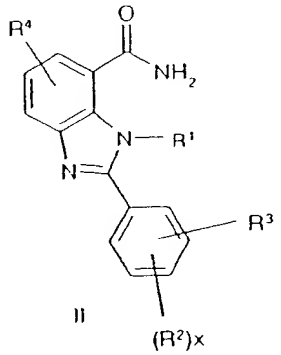
Please amend claims 1-3 and 14 as follows:

Please cancel claims 27, 28 and 30-38

1.(amended) A compound of the formula I or II



I



II

in which

R^1 is hydrogen, or branched and unbranched C_1-C_6-alkyl, it also being possible for one C atom of the alkyl radical to carry OR^{11} or a group R^5, where R^{11} is hydrogen or C_1-C_4-alkyl, and

R^2 is hydrogen, chlorine, bromine, iodine, fluorine, CF_3, nitro, $NHCOR^{21}$, $NR^{22}R^{23}0H$, O-C_1-C_4-alkyl, O-C_1-C_4-alkylphenyl, NH_2, or phenyl, it also being possible for the phenyl rings to be substituted by at most two radicals R^{24}, and R^{21} and R^{22} independently of one another are hydrogen or C_1-C_4-alkyl and R^{23} is hydrogen, C_1-C_4-alkyl or phenyl, and R^{24} is OH, C_1-C_6-alkyl, O-C_1-C_4-alkyl, chlorine, bromine, iodine, fluorine, CF_3, nitro or NH_2, and

x may be 0, 1 or 2 and

R^3 is $-D-(F^1)_p-(E)_q-(F^2)_r-G$, where p, q and r may not simultaneously be 0, or is $-E-(D)_u-(F^2)_s-(G)_v$, it also being possible for the radical E to be substituted by one or two radicals A, and if v = 0, E is imidazole, pyrrole, pyridine, pyrimidine, piperazine, pyrazine, pyrrolidine or piperidine, or R^3 is B and

R^4 is hydrogen, chlorine, fluorine, bromine, iodine, branched and unbranched C_1-C_6-alkyl, OH, nitro, CF_3, CN, $NR^{41}R^{42}$, $NH-CO-R^{43}$, or $O-C_1-C_4$-alkyl, where R^{41} and R^{42} independently of one another are hydrogen or C_1-C_4-alkyl and

R^{43} is hydrogen, C_1-C_4-alkyl, C_1-C_4-alkylphenyl or phenyl, and

D is S or O

E is phenyl, imidazole, pyrrole, thiophene, pyridine, pyrimidine, piperazine, pyrazine, furan, thiazole, isoxazole, pyrrolidine, piperidine, or trihydroazepine and

F^1 is a chain of 1 to 8 carbon atoms, it also being possible for one carbon atom of the chain to carry an OH or $O-C_1-C_4$-alkyl group and

F^2 is a chain of 1 to 8 carbon atoms, it also being possible for one carbon atom of the chain to carry an OH or $O-C_1-C_4$-alkyl group and

p may be 0 or 1

q may be 0 or 1, and

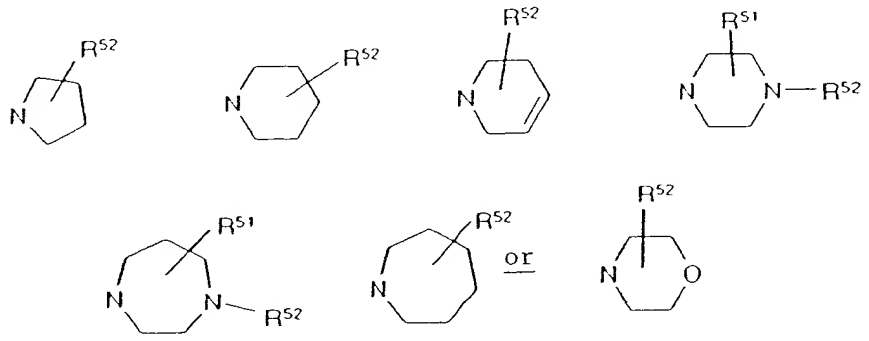
r may be 0 or 1 and

s may be 0 or 1

u may be 0 or 1

v may be 0 or 1

G may be $NR^{51}R^{52}$ or



and

R^{51} is hydrogen or branched and unbranched C_1-C_6-alkyl, or $(CH_2)_t$-K and

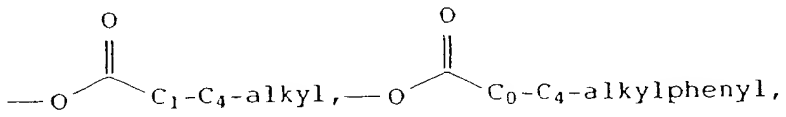
R^{52} is hydrogen, branched and unbranched Cl-C6-alkyl, phenyl,

, $-SO_2R^{53}$, $-(C=N)-R^{53}$, or $-(C=N)-NHR^{53}$

in which

R^{53} may be branched or unbranched O-C_1-C_6-alkyl, phenyl, or branched or unbranched C_1-C_4-alkylphenyl, where in the case of R^{52} and R^{53}, independently of one another, one hydrogen of the C_1-C_6-alkyl radical may be substituted by one of the following radicals: OH, O-C_1-C_4-alkyl, cyclohexyl, cyclopentyl, tetrahydronaphthyl, cyclopropyl, cyclobutyl, cycloheptyl, naphthyl and phenyl, it also being possible for the

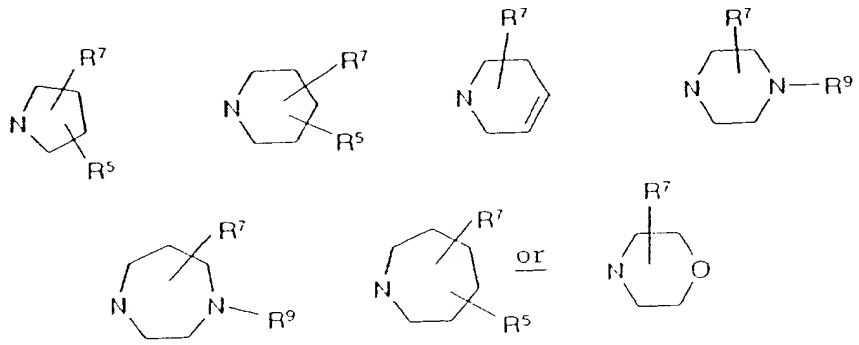
carbocycles of the radicals R^{52} and R^{53} independently of one another to carry one or two of the following radicals: branched or unbranched C_1-C_6-alkyl, branched or unbranched O-C_1-C_4-alkyl, OH, F, C1, Br, I, CF_3, NO_2, NH_2, CN, COOH, $COOC_1$-C_4-alkyl, C_1-C_4-alkylamino, $CC1_3$, C_1-C_4-dialkylamino, SO_2-C_1-C_4- alkyl, SO_2phenyl, $CONH_2$, CONH-C_1-C_4-alkyl, CONHphenyl, CONH-C_1-C_4-alkylphenyl, $NHSO_2$-C_1-C_4-alkyl, $NHSO_2$phenyl, S-C_1-C_4-alkyl,



CHO, CH_2-O-C_1-C_4-alkyl, -CH_2O-C_1-C_4-alkylphenyl, -CH_2OH, -SO-C_1-C_4-alkyl, -SO-C_1-C_4-alkylphenyl, -SO_2NH_2, -SO_2NH- C_1-C_4-alkyl

[and two radicals form] or two radicals form a bridge -O-$(CH_2)_{1,2}$-O-,

B may be



and

A may be hydrogen, chlorine, bromine, iodine, fluorine, CF_3, nitro, OH, O-C_1-C_4-alkyl, O-C_1-C_4-alkylphenyl, NH_2, branched and unbranched C_1-C_6-alkyl,

CN, or NH-CO-R^{33}, where R^{33} is hydrogen, C_1-C_4-alkyl or phenyl and

R^{31} is hydrogen, C_1-C_6-alkyl, or $(CH_2)_t$-K and

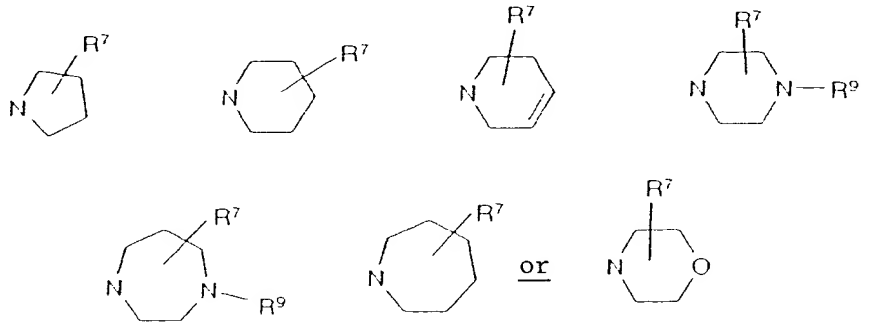
R^{32} is hydrogen, C_1-C_6-alkyl, -CO-R^8, SO_2-R^8, -(C=N)=R^8-CO-NHR^8, -CO-OR^8 [and] or -(C=N)-NHR^8 and

R^{33} is hydrogen [and] or C_1-C_4-alkyl and

t is 0,1,2,3, or 4 and

K is a phenyl which may carry at most two [radicals R, is] substituents on the ring, comprising $NR^{k1}R^{k2}$ [(where] wherein R^{k1} and R^{k2} are as defined for R^{41} and R^{42} respectively[)], NH-C_1-C_4-alkylphenyl, pyrrolidine, piperidine, 1,2, 5, 6-tetrahydropyridine, morpholine, trihydroazepine, piperazine, which may also be substituted by an alkyl radical C_1-C_6-alkyl, [and] or homopiperazine, which may also be substituted by an alkyl radical C_1-C_6-alkyl, and

R^5 may be hydrogen, C_1-C_6-alkyl, or NR_7R_9 and



and

R^7 is hydrogen, C_1-C_6-alkyl, C_1-C_4-alkylphenyl, or phenyl, it also being possible for the rings to be substituted by up to two radicals R^{71}, and

R^{71} is OH, C_1-C_6-alkyl, O-C_1-C_4-alkyl, chlorine, bromine, iodine, fluorine, CF_3, nitro, or NH_2, and

R^8 is hydrogen, C_1-C_6-alkyl, phenyl, or C_1-C_4-alkylphenyl, it also being possible for the ring to be substituted by up to two radicals R^{81}, and

R^{81} is OH, C_1-C_6-alkyl, O-C_1-C_4-alkyl, chlorine, bromine, iodine, fluorine, CF_3, nitro, or NH_2 and

R^9 is hydrogen, $COCH_3$, CO-O-C_1-C_4-alkyl, $COCF_3$, branched and unbranched C_1-C_6-alkyl, it being possible for one or two hydrogens of the C_1-C_6-alkyl radical to be substituted in each case by one of the following radicals: OH, O-C_1-C_4-alkyl and phenyl, and for the phenyl ring also to carry one or two of the following radicals: iodine, chlorine, bromine, fluorine, branched and unbranched C_1-C_6-alkyl, nitro, amino, C_1-C_4-alkylamino, C_1-C_4-dialkylamino, OH, O-C_1-C4-alkyl, CN, CF_3, or SO_2-C_1-C_4-alkyl,

[and the tautomeric forms, possible enantiomeric and diastereomeric forms thereof, the prodrug thereof and pharmacologically tolerated salts] or a tautomeric form, a possible enantiomeric or disasteriomeric form, a prodrug or

pharmacologically tolerated salt thereof.

2.(amended) A compound of the formula I or II as claimed in claim 1 in which

R^1 is hydrogen, branched and unbranched C_1-C_6-alkyl, it also being possible for one C atom of the alkyl radical to carry OR^{11} or a group R^5, where

R^{11} is hydrogen or C_1-C_4-alkyl, and

R^2 is hydrogen, chlorine, fluorine, bromine, iodine, branched and unbranched C_1-C_6-alkyl, nitro, CF_3, CN, $NR^{21}R^{22}$, NH-CO-R^{23}, OR^{21}, where

R^{21} and R^{22} are, independently of one another, hydrogen or C_1-C_4-alkyl, arid

R^{23} is hydrogen, C_1-C_4-alkyl or phenyl, and

R^3 is -O-$(CH_2)_o$-$(CHR^{31})_m$-$(CH_2)_n$-R^5, where

R^{31} is hydrogen, C_1-C_4-alkyl, OH and O-C_1-C_4-alkyl,

m,o are, independently of one another, 0, 1 or 2, and

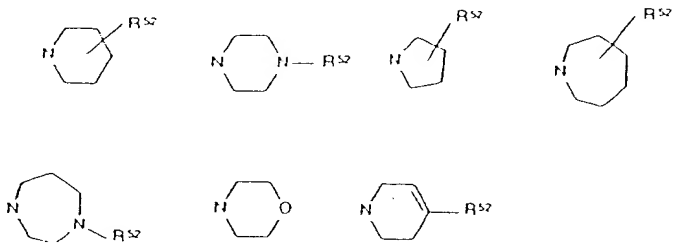
n is 1, 2, 3 or 4 and

R^4 is hydrogen, branched and unbranched C_1-C_6-alkyl, chlorine, bromine, fluorine, nitro, cyano, $NR^{41}R^{42}$ NH-CO-R^{43} OR^{41} where

R^{41} and R^{42} are, independently of one another, hydrogen or C_1-C_4-alkyl, and

R^{43} is C_1-C_4-alkyl or phenyl, and

R^5 is $NR^{51}R^{52}$ or one of the following radicals



where

R^{51} is hydrogen and branched and unbranched C_1-C_6-alkyl, and

R^{52} is hydrogen, branched and unbranched C_1-C_6-alkyl phenyl,

O

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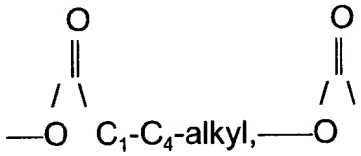
/ \

R^{53}, $-SO_2R^{53}$, in which

R^{53} is branched or unbranched O-C_1-C_6-alkyl, phenyl, branched or unbranched C_1-C_4-alkyl-phenyl, where one hydrogen in the C_1-C_6-alkyl radical in R^{52} and R^{53} can, independently of one another, be substituted by one of the following radicals: OB, O-C_1-C_4-alkyl, cyclohexyl, cyclopentyl, tetrahydronaphthyl, cyclopropyl, cyclobutyl, cycloheptyl, naphthyl and phenyl, where the carbocycles of the R^{52} and R^{53} radicals may also, independently of one another, carry one or two of the following radicals: branched or unbranched C_1-C_6-alkyl, branched or unbranched O-C_1-C_4-alkyl, OH, F, C1, Br, I, CF_3, NO_2, NH_2, CN, COOH, $COOC_1$-C_4-alkyl, C_1-C_4-alkylamino, $CC1_3$, C_1-C_4-dialkylamino, SO_2-C_1-C_4-alkyl, SO_2phenyl,

$CONH_2$, CONH-C_1-C_4-alkyl, CONHphenyl, CONH-C_1-C_4-alkyl-phenyl, $NHSO_2$-C_1-C_4-alkyl, $NBSO_2$phenyl, S-C_1-C_4-alkyl,



—O C_1-C_4-alkyl,——O C_0-C_4-alkyl-phenyl,

CHO, CH_2-O-C_1-C_4-alkyl, -CH_2O-C_1-C_4-alkyl-phenyl, -CH_2OH, -SO-C_1-C_4-alkyl, -SO-C_1-C_4-alkyl-phenyl, SO_2NH_2, -SO_2NH-C_1-C_4-alkyl and two radicals form a bridge -O-$(CH_2)_{1,2}$-O-,

[and the tautomeric form, possible enantiomeric and diastereomeric forms thereof, the prodrugs thereof, and possible physiologically tolerated salts] or a tautomeric form, a possible enantiomeric or disasteriomeric form, a prodrug or pharmacologically tolerated salt thereof.

3.(amended) A compound of the formula I or II as claimed in claim 1 in which

R^1 is hydrogen, branched and unbranched C_1-C_6-alkyl, it also being possible for one C atom of the alkyl radical to carry OR^{11} or a group R^5, where

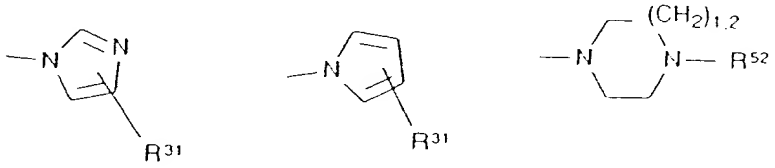
R^{11} is hydrogen or C_1-C_4-alkyl, and

R^2 is hydrogen, chlorine, fluorine, bromine, iodine, branched and unbranched C_1-C_6-alkyl, nitro, CF_3, CN, $NR^{21}R^{22}$, NH-CO-R^{23}, OR^{21}, where

R^{21} and R^{22} independently of one another are hydrogen or

C_1-C_4-alkyl and

R^3 is



and

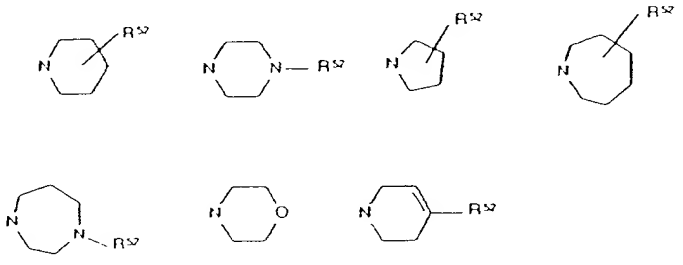
R^{31} is hydrogen, CHO and $-(CH_2)_o-(CHR^{32})_m-(CH_2)_n-R^5$, where R^{32} is hydrogen, C_1-C_4-alkyl, OH and O-C_1-C_4-alkyl, m,o independently of one another are 0, 1 or 2 and n is 1, 2, 3 or 4, and

R^4 is hydrogen, branched and unbranched C_1-C_6-alkyl, chlorine, bromine, fluorine, nitro, cyano, $NR^{41}R^{42}$ NH-CO-R^{43}, OR^{41}, where

$R^{41}$and R^{42} independently of one another are hydrogen or C_1-C_4-alkyl and

R^{43} is C_1-C_4-alkyl or phenyl, and

R^5 is $NR^{51}R^{52}$ or one of the radicals below



where

R^{51} is hydrogen and branched and unbranched and C_1-C_6-alkyl and

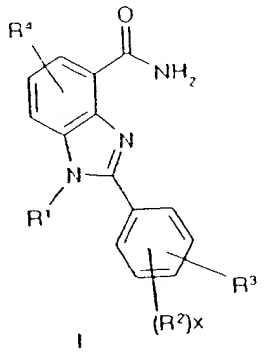
R^{52} is hydrogen, $COCH_3$, CO-O-C_1-C_4-alkyl, $COCF_3$, branched and unbranched C_1-C_6-alkyl, it being possible for one hydrogen of the C_1-C_6-alkyl radical to be substituted by one of the following radicals: OH, O-C_1-C_4-alkyl and phenyl and for the phenyl ring also to carry one or two of the following radicals: chlorine, bromine, fluorine, branched and unbranched C_1-C_4-alkyl, nitro, amino, C_1-C_4-alkylamino, C_1-C_4-dialkylamino, OH, O-C_1-C_4-alkyl, CN, SO_2-C_1-C_4-alkyl,

[and the tautomeric forms, possible enantiomeric and diastereomeric forms thereof, the prodrug thereof, and possible physiologically tolerated salts] <u>or a tautomeric form, a possible enantiomeric or disasteriomeric form, a prodrug or pharmacologically tolerated salt thereof</u>.

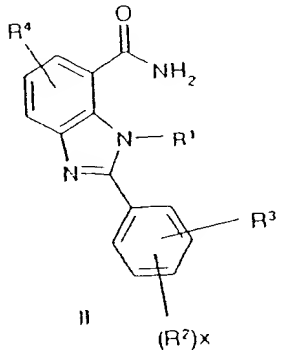
14.(amended) The method as claimed in claim 11 wherein the disorder is [stroke and] <u>stroke or</u> craniocerebral trauma.

COPY OF ALL CLAIMS

1. A compound of the formula I or II



I



II

in which

R^1 is hydrogen, or branched and unbranched C_1-C_6-alkyl, it also being possible for one C atom of the alkyl radical to carry OR^{11} or a group R^5, where R^{11} is hydrogen or C_1-C_4-alkyl, and

R^2 is hydrogen, chlorine, bromine, iodine, fluorine, CF_3, nitro, $NHCOR^{21}$, $NR^{22}R^{23}0H$, O-C_1-C_4-alkyl, O-C_1-C_4-alkylphenyl, NH_2, or phenyl, it also being possible for the phenyl rings to be substituted by at most two radicals R^{24}, and R^{21} and R^{22} independently of one another are hydrogen or C_1-C_4-alkyl and R^{23} is hydrogen, C_1-C_4-alkyl or phenyl, and R^{24} is OH, C_1-C_6-alkyl, O-C_1-C_4-alkyl, chlorine, bromine, iodine, fluorine, CF_3, nitro or NH_2, and

x may be 0, 1 or 2 and

R^3 is -D-$(F^1)_p$-$(E)_q$-$(F^2)_r$-G, where p, q and r may not simultaneously be 0, or is -E-$(D)_u$-$(F^2)_s$-$(G)_v$, it also being possible for the radical E to be substituted by one or two radicals A, and if v = 0, E is imidazole, pyrrole, pyridine, pyrimidine, piperazine, pyrazine, pyrrolidine or piperidine, or R^3 is B and

R^4 is hydrogen, chlorine, fluorine, bromine, iodine, branched and unbranched C_1-C_6-alkyl, OH, nitro, CF_3, CN, $NR^{41}R^{42}$, NH-CO-R^{43}, or O-C_1-C_4-alkyl, where R^{41} and R^{42} independently of one another are hydrogen or C_1-C_4-alkyl and R^{43} is hydrogen, C_1-C_4-alkyl, C_1-C_4-alkylphenyl or phenyl, and

D is S or O

E is phenyl, imidazole, pyrrole, thiophene, pyridine, pyrimidine, piperazine, pyrazine, furan, thiazole, isoxazole, pyrrolidine, piperidine, or trihydroazepine and

F^1 is a chain of 1 to 8 carbon atoms, it also being possible for one carbon atom of the chain to carry an OH or O-C_1-C_4-alkyl group and

F^2 is a chain of 1 to 8 carbon atoms, it also being possible for one carbon atom of the chain to carry an OH or O-C_1-C_4-alkyl group and

p may be 0 or 1

q may be 0 or 1, and

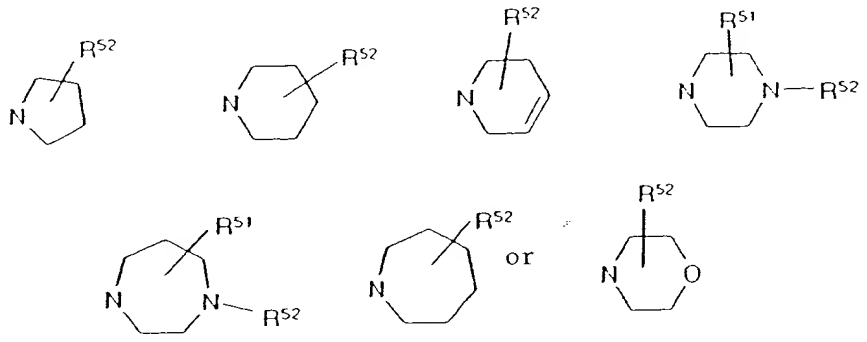
r may be 0 or 1 and

s may be 0 or 1

u may be 0 or 1

v may be 0 or 1

G may be $NR^{51}R^{52}$ or



and

R^{51} is hydrogen or branched and unbranched C_1-C_6-alkyl, or $(CH_2)_t$-K and

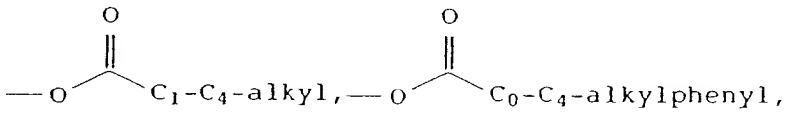
R^{52} is hydrogen, branched and unbranched Cl-C6-alkyl, phenyl,

, $-SO_2R^{53}$, $-(C=N)-R^{53}$, or $-(C=N)-NHR^{53}$

in which

R^{53} may be branched or unbranched O-C_1-C_6-alkyl, phenyl, or branched or unbranched C_1-C_4-alkylphenyl, where in the case of R^{52} and R^{53}, independently of one another, one hydrogen of the C_1-C_6-alkyl radical may be substituted by one of the following radicals: OH, O-C_1-C_4-alkyl, cyclohexyl, cyclopentyl, tetrahydronaphthyl, cyclopropyl, cyclobutyl, cycloheptyl, naphthyl and phenyl, it also being possible for the

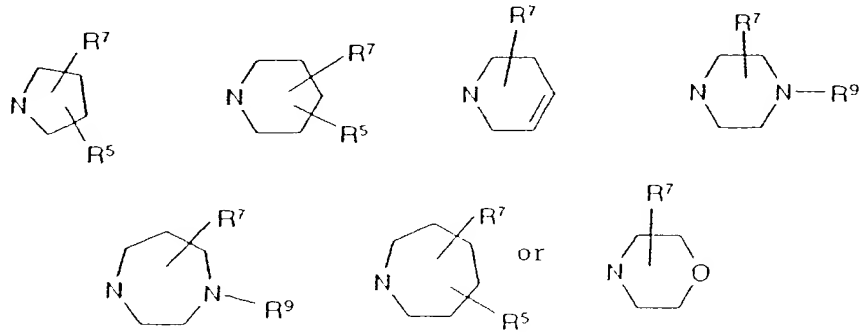
carbocycles of the radicals R^{52} and R^{53} independently of one another to carry one or two of the following radicals: branched or unbranched C_1-C_6-alkyl, branched or unbranched O-C_1-C_4-alkyl, OH, F, C1, Br, I, CF_3, NO_2, NH_2, CN, COOH, $COOC_1$-C_4-alkyl, C_1-C_4-alkylamino, $CC1_3$, C_1-C_4-dialkylamino, SO_2-C_1-C_4- alkyl, SO_2phenyl, $CONH_2$, CONH-C_1-C_4-alkyl, CONHphenyl, CONH-C_1-C_4-alkylphenyl, $NHSO_2$-C_1-C_4-alkyl, $NHSO_2$phenyl, S-C_1-C_4-alkyl,



CHO, CH_2-O-C_1-C_4-alkyl, -CH_2O-C_1-C_4-alkylphenyl, -CH_2OH, -SO-C_1-C_4-alkyl, -SO-C_1-C_4-alkylphenyl, -SO_2NH_2, -SO_2NH- C_1-C_4-alkyl

or two radicals form a bridge -O-$(CH_2)_{1,2}$-O-,

B may be



and

A may be hydrogen, chlorine, bromine, iodine, fluorine, CF_3, nitro, OH, O-C_1-C_4-alkyl, O-C_1-C_4-alkylphenyl, NH_2, branched and unbranched C_1-C_6-alkyl, CN, or NH-CO-R^{33}, where R^{33} is hydrogen, C_1-C_4-alkyl or phenyl and

R^{31} is hydrogen, C_1-C_6-alkyl, or $(CH_2)_t$-K and

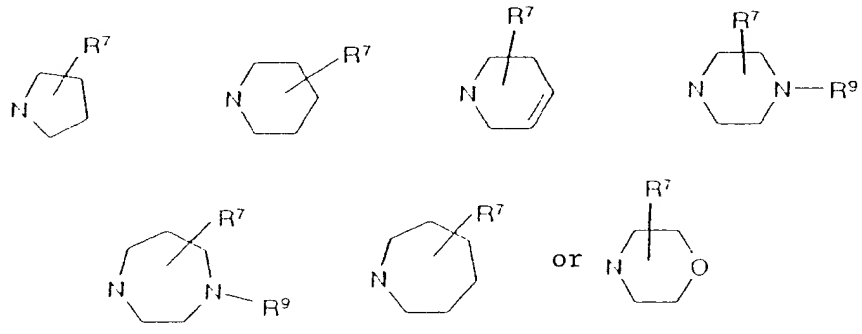
R^{32} is hydrogen, C_1-C_6-alkyl, -CO-R^8, SO_2-R^8, -(C=N)=R^8-CO-NHR^8, -CO-OR^8 or -(C=N)-NHR^8 and

R^{33} is hydrogen or C_1-C_4-alkyl and

t is 0,1,2,3, or 4 and

K is a phenyl which may carry at most two substituents on the being, comprising $NR^{k1}R^{k2}$ wherein R^{k1} and R^{k2} re as defined for R^{41} and R^{42} respectively, NH-C1-C_4-alkylphenyl, pyrrolidine, piperidine, 1,2, 5, 6-tetrahydropyridine, morpholine, trihydroazepine, piperazine, which may also be substituted by an alkyl radical C_1-C_6-alkyl, or homopiperazine, which may also be substituted by an alkyl radical C_1-C_6-alkyl, and

R^5 may be hydrogen, C_1-C_6-alkyl, or NR_7R_9 and



and

R^7 is hydrogen, C_1-C_6-alkyl, C_1-C_4-alkylphenyl, or phenyl, it also being possible for the rings to be substituted by up to two radicals R^{71}, and

R^{71} is OH, C_1-C_6-alkyl, O-C_1-C_4-alkyl, chlorine, bromine, iodine, fluorine, CF_3, nitro, or NH_2, and

R^8 is hydrogen, C_1-C_6-alkyl, phenyl, or C_1-C_4-alkylphenyl, it also being possible for the ring to be substituted by up to two radicals R^{81}, and

R^{81} is OH, C_1-C_6-alkyl, O-C_1-C_4-alkyl, chlorine, bromine, iodine, fluorine, CF_3, nitro, or NH_2 and

R^9 is hydrogen, $COCH_3$, CO-O-C_1-C_4-alkyl, $COCF_3$, branched and unbranched C_1-C_6-alkyl, it being possible for one or two hydrogens of the C_1-C_6-alkyl radical to be substituted in each case by one of the following radicals: OH, O-C_1-C_4-alkyl and phenyl, and for the phenyl ring also to carry one or two of the following radicals: iodine, chlorine, bromine, fluorine, branched and unbranched C_1-C_6-alkyl, nitro, amino, C_1-C_4-alkylamino, C_1-C_4-dialkylamino, OH, O-C_1-C4-alkyl, CN, CF_3, or SO_2-C_1-C_4-alkyl,

or a tautomeric form, a possible enantiomeric or disasteriomeric form, a prodrug or pharmacologically tolerated salt thereof.

2. A compound of the formula I or II as claimed in claim 1 in which

R^1 is hydrogen, branched and unbranched C_1-C_6-alkyl, it also being possible for one C atom of the alkyl radical to carry OR^{11} or a group R^5, where

R^{11} is hydrogen or C_1-C_4-alkyl, and

R^2 is hydrogen, chlorine, fluorine, bromine, iodine, branched and unbranched C_1-C_6-alkyl, nitro, CF_3, CN, $NR^{21}R^{22}$, NH-CO-R^{23}, OR^{21}, where

R^{21} and R^{22} are, independently of one another, hydrogen or C_1-C_4-alkyl, arid

R^{23} is hydrogen, C_1-C_4-alkyl or phenyl, and

R^3 is -O-$(CH_2)_o$-$(CHR^{31})_m$-$(CH_2)_n$-R^5, where

R^{31} is hydrogen, C_1-C_4-alkyl, OH and O-C_1-C_4-alkyl,

m,o are, independently of one another, 0, 1 or 2, and

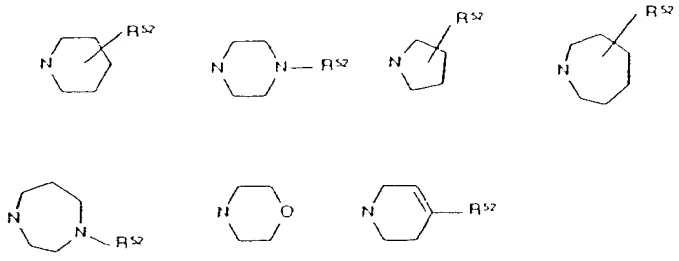
n is 1, 2, 3 or 4 and

R^4 is hydrogen, branched and unbranched C_1-C_6-alkyl, chlorine, bromine, fluorine, nitro, cyano, $NR^{41}R^{42}$ NH-CO-R^{43} OR^{41} where

R^{41} and R^{42} are, independently of one another, hydrogen or C_1-C_4-alkyl, and

R^{43} is C_1-C_4-alkyl or phenyl, and

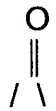
R^5 is $NR^{51}R^{52}$ or one of the following radicals



where

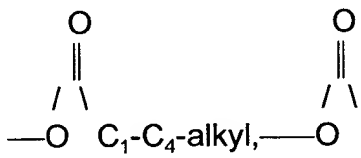
R^{51} is hydrogen and branched and unbranched C_1-C_6-alkyl, and

R^{52} is hydrogen, branched and unbranched C_1-C_6-alkyl phenyl,



R^{53}, $-SO_2R^{53}$, in which

R^{53} is branched or unbranched O-C_1-C_6-alkyl, phenyl, branched or unbranched C_1-C_4-alkyl-phenyl, where one hydrogen in the C_1-C_6-alkyl radical in R^{52} and R^{53} can, independently of one another, be substituted by one of the following radicals: OB, O-C_1-C_4-alkyl, cyclohexyl, cyclopentyl, tetrahydronaphthyl, cyclopropyl, cyclobutyl, cycloheptyl, naphthyl and phenyl, where the carbocycles of the R^{52} and R^{53} radicals may also, independently of one another, carry one or two of the following radicals: branched or unbranched C_1-C_6-alkyl, branched or unbranched O-C_1-C_4-alkyl, OH, F, C1, Br, I, CF_3, NO_2, NH_2, CN, COOH, $COOC_1$-C_4-alkyl, C_1-C_4-alkylamino, $CC1_3$, C_1-C_4-dialkylamino, SO_2-C_1-C_4-alkyl, SO_2phenyl, $CONH_2$, CONH-C_1-C_4-alkyl, CONHphenyl, CONH-C_1-C_4-alkyl-phenyl, $NHSO_2$-C_1-C_4-alkyl, $NBSO_2$phenyl, S-C_1-C_4-alkyl,



—O C_1-C_4-alkyl,——O C_0-C_4-alkyl-phenyl,

CHO, CH_2-O-C_1-C_4-alkyl, -CH_2O-C_1-C_4-alkyl-phenyl, -CH_2OH, -SO-C_1-C_4-alkyl, -SO-C_1-C_4-alkyl-phenyl, SO_2NH_2, -SO_2NH-C_1-C_4-alkyl and two radicals form a bridge -O-$(CH_2)_{1,2}$-O-,

or a tautomeric form, a possible enantiomeric or disasteriomeric form, a prodrug or pharmacologically tolerated salt thereof.

3. A compound of the formula I or II as claimed in claim 1 in which

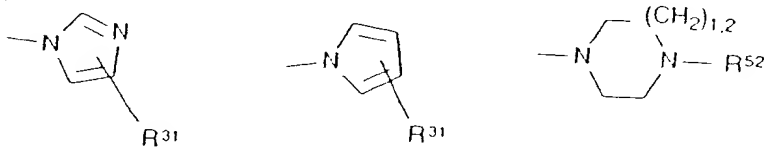
R^1 is hydrogen, branched and unbranched C_1-C_6-alkyl, it also being possible for one C atom of the alkyl radical to carry OR^{11} or a group R^5, where

R^{11} is hydrogen or C_1-C_4-alkyl, and

R^2 is hydrogen, chlorine, fluorine, bromine, iodine, branched and unbranched C_1-C_6-alkyl, nitro, CF_3, CN, $NR^{21}R^{22}$, NH-CO-R^{23}, OR^{21}, where

R^{21} and R^{22} independently of one another are hydrogen or C_1-C_4-alkyl and

R^3 is



and

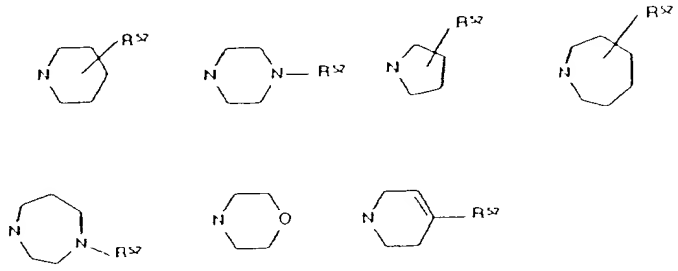
R^{31} is hydrogen, CHO and -$(CH_2)_o$-$(CHR^{32})_m$-$(CH_2)_n$-R^5, where R^{32} is hydrogen, C_1-C_4-alkyl, OH and O-C_1-C_4-alkyl, m,o independently of one another are 0, 1 or 2 and n is 1, 2, 3 or 4, and

R^4 is hydrogen, branched and unbranched C_1-C_6-alkyl, chlorine, bromine, fluorine, nitro, cyano, $NR^{41}R^{42}$ NH-CO-R^{43}, OR^{41}, where

$R^{41}$and R^{42} independently of one another are hydrogen or C_1-C_4-alkyl and

R^{43} is C_1-C_4-alkyl or phenyl, and

R^5 is $NR^{51}R^{52}$ or one of the radicals below



where

R^{51} is hydrogen and branched and unbranched and C_1-C_6-alkyl and

R^{52} is hydrogen, $COCH_3$, CO-O-C_1-C_4-alkyl, $COCF_3$, branched and unbranched C_1-C_6-alkyl, it being possible for one hydrogen of the C_1-C_6-alkyl radical to be substituted by one of the following radicals: OH, O-C_1-C_4-alkyl and phenyl and for the phenyl ring also to carry one or two of the following radicals: chlorine, bromine, fluorine, branched and unbranched C_1-C_4-alkyl, nitro, amino, C_1-C_4-alkylamino, C_1-C_4-dialkylamino, OH, O-C_1-C_4-alkyl, CN, SO_2-C_1-C_4-alkyl,

or a tautomeric form, a possible enantiomeric or disasteriomeric form, a prodrug or pharmacologically tolerated salt thereof.

4. A compound as claimed in claim 1, where R^2 is in position 3 and R^3 is in position 4 or R^2 is in position 4 and R^3 is in position 3 relative to the benzimidazole ring.

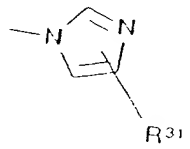
5. A compound as claimed in claim 1, where R^1 and R^4 are hydrogen.

6. A compound as claimed in claim 1, where

R^2 is hydrogen, branched or unbranched C_1-C_6-alkyl, nitro, CN, NH_2, O-C_1-C_4-alkyl.

7. A compound as claimed in claim 1 where

(i) for R^3 being

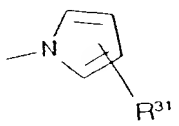


R^{31} is hydrogen or -$(CH_2)_p$-R^5, where

p is 1 or 2 and

R^{52} may be hydrogen, branched and unbranched C_1-C_6-alkyl, where one hydrogen of the C_1-C_6-alkyl radical may be substituted by one of the following radicals: OH, O-C_1-C_4-alkyl and phenyl, and where the phenyl ring may also carry one or two of the following radicals: chlorine, bromine, fluorine, branched and unbranched C_1-C_4-alkyl, nitro, amino, C_1-C_4-alkylamino, C_1-C_4- dialkylamino, OH, O-C_1-C_4-alkyl, CN, SO_2-C_1-C_4-alkyl;

(ii) for R^3 being

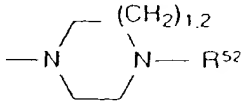


R^{31} is hydrogen or $-(CH_2)_p-R^5$, where

p is 1 or 2 and

R^{52} may be hydrogen, branched and unbranched C_1-C_6-alkyl, where one hydrogen of the C_1-C_6-alkyl radical may be substituted by one of the following radicals: OH, O-C_1-C_4-alkyl and phenyl, and where the phenyl ring may also carry one or two of the following radicals: chlorine, bromine, fluorine, branched and unbranched C_1-C_4-alkyl, nitro, amino, C_1-C_4-alkylamino, C_1-C_4- dialkylamino, OH, O-C_1-C_4-alkyl, CN, SO_2-C_1-C_4-alkyl;

and (iii) for R^3 being



where R^{52} is hydrogen, branched and unbranched C_1-C_6-alkyl, where one hydrogen of the C_1-C_6-alkyl radical may be substituted by one of the following radicals: OH,

O-C_1-C_4-alkyl and phenyl, and where the phenyl ring may also carry one or two of the following radicals: chlorine, bromine, fluorine, branched and unbranched C_1-C_4-alkyl,

nitro, amino, C_1-C_4-alkylamino, C_1-C_4-dialkylamino, OH, O-C_1-C_4-alkyl, CN, SO_2-C_1-C_4-alkyl.

8. A compound as claimed in claim 1, where R^3 is $-O-(CH_2)_p-R^5$ with p equal to 2, 3 or 4.

9. A compound as claimed in claim 1, where R^5 is a 6-membered ring and R^{52} is an optionally substituted phenyl ring.

10. A drug comprising besides conventional vehicles and ancillary substances a compound as claimed in claim 1.

11. A method for treating a disorder in which pathologically elevated PARP activities occur, said method comprising administering an effective amount of a compound of the formula I as claimed in claim 1 to a mammal suffering from said disorder.

12. The use of compounds of the formula I as claimed in claim 11 wherein the disorder is a neurodegenerative disease or involves neuronal damage.

13. The method as claimed in claim 12, wherein the neurodegenerative disease or neuronal damage is induced by ischemia, trauma or massive bleeding.

14. The method as claimed in claim 11 wherein the disorder is stroke or craniocerebral trauma.

15. The method as claimed in claim 11 wherein the disorder is Alzheimer's disease and Huntington's disease.

16. The method as claimed in claim 11 wherein the disorder is damage due to ischemia.

17. The method as claimed in claim 11 wherein the disorder is epilepsy.

18. The method as claimed in claim 11 wherein the disorder is damage to the kidneys after renal ischemia, damage caused by drug therapy or damage resulting after kidney transplants.

19. The method as claimed in claim 11 wherein the disorder is damage to the heart after cardiac ischemia.

20. The method as claimed in claim 11 wherein the disorder is a microinfarcts.

21. The method as claimed in claim 11 wherein the disorder is under vascularization of critically narrowed coronary arteries.

22. The method as claimed in claim 11 wherein the disorder is an acute myocardial infarct and damage during an after medical or mechanical lysis thereof.

23. The method as claimed in claim 11 wherein the disorder is a tumor or metastasis l thereof.

24. The method as claimed in claim 11 wherein the disorder is sepsis of multi-organ failure.

25. The method as claimed in claim 11 wherein the disorder is an immunological disease.

26. The method as claimed in claim 11 wherein the disorder is diabetes mellitus.